



## To Study S.CRP & S.LDH Levels in Snake Bite Patients as a Markers of Hemotoxicity

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### Introduction

Snake bite is considered as one of the medical emergency, either hemotoxic, neurotoxic, cytotoxic or a combination of these. The consequence of envenomation can range from minimal local tissue injury to multi-organ dysfunction. It is suspected that snake venom functions as an acute-phase reactant and interacts with target cells such as macrophages that release inflammatory mediators such as IL(Interleukin)-6 and 8. IL6 is believed to act on the liver, increasing acute phase reactants' production like c-reactive protein, ESR, serum amyloid, haptoglobin, etc<sup>1</sup>. Hemolysis, a typical manifestation of snake bite is thought to generate phospholipase, an essential component of snake venom. Serum lactate dehydrogenase (LDH) levels found to be associate well with snake

venom hemotoxicity and snake bite envenomation severity<sup>2</sup>. The ability to detect grade of envenomation at presentation is that of challenge and novel markers for the same would be a good guide for treatment as well at prognosis. Snakes are categorized into four families; these are Elapidae, Hydrophidae, Atractaspididae and Viperidae. In Indian subcontinent major families found to be Elapidae, which includes Common cobra, king cobra and krait, Viperidae that includes Russells viper, Pit viper and Saw-scaled viper and Hydrophidae.<sup>3</sup>

Of the 70 poisonous species in India majority of bites and consequent mortality is attributable to 5 species which are King Cobra (Ophiophagus Hannah), Common Cobra (NajaNaja), Russells viper (Daberia Ruselli), Saw-Scaled viper (Echis Carinatae) and Krait (Bungarus Caeruleus).<sup>3</sup>

### Grading of severity of envenomation

Severity of envenomation is graded by the following scale.<sup>4</sup>

No envenomation:	
Local manifestations	Mild pain
Systemic manifestations	None
Laboratory findings	None

<b>Mild envenomation</b>	
Local manifestation	Swelling, erythema or echymosis confined to the site of bite
Systemic manifestations	None
Laboratory findings	None
<b>Moderate envenomation</b>	
Local manifestation	Progression of swelling, erythema or ecchymosis beyond the site of bite
Systemic manifestations	Non life threatening signs and symptoms. Perioral and peripheral paresthesia, nausea, vomiting, diarrhea, ptosis, diplopia.
Laboratory findings	Mildly abnormal coagulation profile with no features of systemic bleeding. Mildly abnormal other laboratory tests.
<b>Severe envenomation</b>	
Local manifestation	Rapid swelling, erythema echymosis involving the entire part or body
Systemic manifestation	Tachycardia, hypotension, tachypnoea, respiratory paralysis, fasciculation, altered mental status, seizures
Laboratory findings	Systemic bleeding or markedly altered coagulation profile, unmeasurable INR, APTT and platelet count <20,000

### Aims and Objectives

1. To study the role of acute inflammatory marker serum CRP and serum LDH in cases of snake bite envenomation.
2. To study the prediction of early prognosis with the help of the above markers in snake bite patients

### Materials & Methods

#### Source of Data

The data for the study is collected from patients attended to Great Eastern Medical School & Hospital, Ragolu, Srikakulam with a history of snakebite.

**Study Period:** October 2018 to march 2020.

**Study Design:** Cross sectional observational study.

**Sample Size:** 50 patients were selected for the study using purposive sampling technique based on inclusion and exclusion criteria after obtaining informed consent. On admission vital signs and site of bite were recorded.

Patients with history suggestive of snakebite, the following lab tests were included. Complete blood picture, ESR (erythrocyte sedimentation rate), PCV (packed cell volume), Urine routine and micro analysis, Serum CRP and LDH, PT-INR (prothrombin time with international normalized ratio), APTT (activated partial thromboplastin time) all of which were done at admission and following 24 hours thereafter.

Clotting time, bleeding time and A 20 minute

whole blood clotting test were repeated every 6<sup>th</sup> hourly for the 1st 24 hours of hospital admission. Dry bites were defined as patients with a history of snakebite but without signs or symptoms of local or systemic envenomation or lab abnormalities even after 24 hours of observation in the hospital. Patients were thereafter divided into no, mild, moderate and severe envenomation group based on a predetermined scale.

The above values were noted and a relation was drawn with the values of serum LDH and CRP levels.

#### Inclusion Criteria

Patients with alleged history of snakebite or unknown bites but with symptoms and signs compatible with snake bite envenomation

#### Exclusion Criteria

Any bite not caused by a snake.

Patients who received ASV prior to hospitalization.

Patients with history of known vasculitis, bleeding disorders, liver diseases, acute myocardial ischemia.

#### Data Analysis

Data entered in Excel sheet and analysed using SPSS 20 software. Collected data was analyzed by frequency, percentage, mean, standard deviation and P value calculated by Student t test and chi square test. MS word, Tables & graphs were used to show the data. P value <0.05 is considered as statistically significant.

**Results & Discussion**

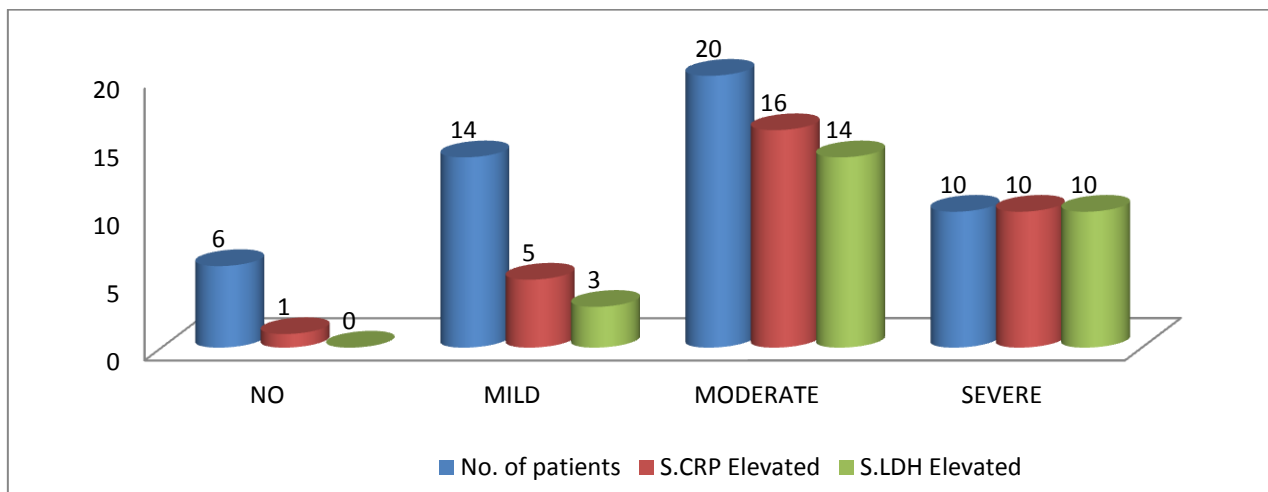
- The mean age of our study is 39.8±9.76.  
 - Manifestations of envenomation are present in 46 patients. Of which 30 patients (65.21%) had hemotoxic manifestations. 14 patients(30.43%)

had local envenomation. 2 patients (4.34%) had neurotoxic manifestations. In a study done in Bangalore by Harshavardhana HS et al.<sup>7</sup>, 60% were showed prolongation in the WBCT.

**Table 1:** Grade of Envenomation and its relation with S. CRP and LDH values

Grade of Envenomation	No. of patients	Percentage	CRP Elevated	Percentage	LDH Elevated	Percentage
No	06	12%	1	16.66%	0	0%
Mild	14	28%	5	35.71%	3	21.42%
Moderate	20	40%	16	80%	14	70%
Severe	10	20%	10	100%	10	100%
<b>Total</b>	<b>50</b>					

**Figure 1:** Grade of Envenomation and its relation with S. CRP and LDH values



**Table 2:** Polyvalent ASV used and its comparison with S. CRP and LDH

Number of vials of ASV	No. of patients	Percentage%	CRP Elevated	Percentage%	LDH Elevated	Percentage%
NIL	08	16	03	37.5	0	0
<10	13	26	07	53.84	03	23.07
10-20	10	20	06	60	05	50
>30	19	38	15	78.94	16	84.21
<b>TOTAL</b>	<b>50</b>					

In our study 19(38%) of the patients received more than 30 vials of polyvalent ASV. Of these S. CRP & LDH levels are elevated in 15 (78.94%) & 16 (84.21%) respectively whereas 10(20%) received 10-20 vials. Of these S. CRP & LDH

levels elevated in 6 (60%) & 5 (50%) respectively and 13(26%) received less than 10 vials. Of these S. CRP & LDH levels are elevated in 7(53.84%) & 3(23.07%) respectively

**Table 3:** Grades of envenomation and its comparison to S. CRP and LDH in our study group

ENVENOMATION	S. CRP at PRESENTATION	S. CRP AT 24 HOURS	P value of S. CRP between at presentation & at 24hrs	S. LDH AT PRESENTATION	S. LDH AT 24 HOURS	P value of S. LDH between at presentation & at 24hrs
NO	3.10±2.68	3.58±2.84	0.38	145.08±7.98	175.48±21.59	0.0001
MILD	9.86±2.78	15.36±5.88	0.0001	208.06±8.07	268±42.98	0.0001
MODERATE	22.41±15.56	32.37±21.30	0.0089	292.18 ±41.02	324.30±53.78	0.0002
SEVERE	23.01±14.58	33.03±22.48	0.0095	335.75±82.68	370.07±97.19	0.0559
p value between mild and severe envenomation	0.0001	0.0001		0.0001	0.0001	

In our study S.CRP at presentation averages  $9.86 \pm 2.78$  and at 24hrs it is  $15.36 \pm 5.88$  in mild envenomation group whereas in severe group it is around  $23.01 \pm 14.55$  at presentation and raised to  $33.03 \pm 22.48$  with p values 0.0001 & 0.0095 in these groups. S.LDH at presentation averages  $208.06 \pm 8.07$  and at 24hrs it is  $268 \pm 42.98$  in mild envenomation group whereas in severe group it is around  $335.75 \pm 82.68$  at presentation and raised to  $370.07 \pm 97.19$  with p values 0.0001 & 0.0559 in these groups. There will be significant difference for S.CRP & S.LDH at presentation and 24hrs after presentation between mild & severe envenomation with p value 0.0001 in all grades of envenomation. There is statistically significant difference in the S CRP values both at admission and 24 hours later between the mild and severely envenomed group of patients (p value 0.0001) in our study. In a study by Xie Y, et al,<sup>2</sup> in china on victims of pit viper envenomation, patients were divided into mild, moderate and severely envenomed group. A significant difference was found in S.CRP levels between all the 3 groups (p < 0.01).

The difference between the 2 groups among the grades of envenomation could be attributed to higher incidence of pit viper bites, differences in study population as well as systemic envenomation in their study group.

It was also noted that in our study that 4 patients with no features envenomation.

A study done by Bhagwat K, et al.<sup>6</sup> is similar to our study in Maharashtra on 50 patients of snakebite showed elevated S. LDH recordings at the time of admission and 24 hours later in snake bite victims as compared to the control group (p value < 0.05) but our study did not have a control group. However there was found to be no similarity in the values of S.LDH between our study and that of Bhagwat K, et al,<sup>6</sup> (p value 0.325). A study done by Kandaswamy S, et al.<sup>5</sup> in Tamil Nadu involving 30 snakebite victims showed a statistically significant difference (p value 0.01) between S.LDH values recorded in haemotoxic snakebite victims and control group at admission. S. LDH values done at admission in

patients with envenomation were found to be similar between our study and Kandaswamy S, et al.<sup>5</sup> (p value 0.03). This could be because of the similar profile of patients as well grade of envenomation in our group and that of Kandaswamy S, et al<sup>5</sup>.

### Summary

The study was done to study the relationship between hemotoxicity and Serum CRP and LDH levels in snake bite victims.

1. Majority (40%) of our patients presented with features compatible with moderate envenomation
2. Hemotoxic envenomation was the most common manifestation of envenomation in our study group (65.21%)
3. A majority of our patients received 30 or more vials of Polyvalent ASV (38%)
4. S.CRP showed a significant elevation in their levels at admission and 24 hours later with p value of 0.0001, 0.0089, 0.0095 in mild, moderate & severe grades of envenomation respectively.
5. S.LDH showed a significant elevation in their levels at admission and 24 hours later with p value of 0.0001, 0.0002, 0.0559 in mild, moderate & severe grades of envenomation respectively.
6. The values of S.CRP & S.LDH were found to be raised in the severely envenomed group as compared to those with mild envenomation (p value 0.0001).

### Conclusion

1. Most of the patients received more than 30 vials of Polyvalent ASV signifying higher incidence of systemic envenomation in our patients.
2. S.CRP & S. LDH levels showed significant difference at the time of presentation and 24 hrs after the admission in all grades of envenomation.
3. S. CRP & S.LDH was found to be elevated significantly in the severe envenomation group as compared to those with mild

envenomation.

4. Hence S.CRP & LDH levels can serve as markers for hemotoxicity in snake bite victims and may help in predicting prognosis.
5. However, this needs to be studied in a larger population.

## References

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